UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

WYETH, Plaintiff, v. IMPAX LABORATORIES, INC.. Defendant.	Civil Action No. 06-222 (JJF) **PUBLIC VERSION**

IMPAX LABORATORIES, INC.'S MOTION FOR SUMMARY JUDGMENT OF ANTICIPATION AND OBVIOUSNESS

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I. INTRODUCTION

In order to obtain the patents in suit, Wyeth claimed to have discovered a "completely unexpected" solution to the purported problem of how to create an extended release formulation of a highly water soluble drug such as venlafaxine. In fact, however, Wyeth did little more than take an existing extended release formulation of a different drug and replace the active ingredient. REDACTED

In short, Wyeth's patents are invalid because they do not represent an advance—let alone a non-obvious advance—over the prior art. And to the extent the claims are construed even more broadly to encompass virtually *any* extended release formulation, then they are also both anticipated and rendered obvious by prior art disclosing extended release formulations of venlafaxine.

II. STATEMENT OF UNDISPUTED FACTS[1]

A. Wyeth's development of Effexor XR

1. Wyeth obtained a patent on venlafaxine as a treatment for depression.

In 1983, Wyeth filed for a patent on the chemical compound now known as venlafaxine. U.S. Patent No. 4,535,186 (the "'186 patent") issued on August 13, 1985 and will expire on December 13, 2007.[2] The '186 patent's specification explains that venlafaxine is useful to treat depression.[3] Wyeth first marketed Effexor, an immediate-release formulation of venlafaxine, in 1994. Since then, Wyeth has made billions of dollars from sales of venlafaxine.[4]

2. Wyeth developed Effexor XR in order to increase patient convenience.

Wyeth's initial venlafaxine product, Effexor, was an immediate-release formulation

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[1] This Statement of Undisputed Facts is identical to the Statement of Undisputed Facts contained in Impax's contemporaneously-filed Motion for Summary Judgment of Noninfringement, Lack of Written Description, and Lack of Enablement.

[2] Declaration of Mary Matterer in Support of Impax Laboratories, Inc.'s Motions for Summary Judgment, Ex. 1 ('186 patent).

[3] Ex. 1 ('186 patent (cover page)).

[4] *See* Towle Markman Decl., D.I. 194, Ex. A-E (Wyeth annual reports showing revenues from Effexor).

typically taken by patients two or three times a day.[5]

Wyeth began developing a once-a-day formulation of venlafaxine.[6] Wyeth's reason for doing so was straightforward:

Wyeth's 30(b)(6) witness conceded that

Internal Wyeth documents confirm that its extended-release venlafaxine product was nothing more than

3.

Extended release formulation techniques have been known in the art and taught in pharmacy schools since the 1950s. Since then, a limited number of extended-release techniques have been used in countless products with different active ingredients.[10] Wyeth itself has developed and marketed several different extended-release products.[11]

Wyeth began its development of an extended release venlafaxine formulation by

[5] Ex. 2 (excerpt from Effexor XR NDA) at WYETH 004-000299.

[6]

[7]

[8] Ex. 5 (Enever Depo.) at 39:1-7.

[9] Ex. 6 WYETH 004-000326-361 at 330.

[10] *See, e.g.*, *infra* sections II.A.4-5.

[11] *See id.*

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4. Wyeth failed to make extended-release venlafaxine as a hydrogel tablet.

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12 REDACTED

REDACTED

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14 REDACTED

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16 REDACTED

17 Ex. 3 REDACTED

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As the patents-in-suit disclose, the hydrogel tablets Sherman made dissolved too rapidly: "Numerous attempts to produce extended release tablets by hydrogel technology proved to be fruitless because the compressed tablets were either physically unstable (poor compressibility or capping problems) or dissolved too rapidly in dissolution studies."[20] Wyeth eventually concluded that developing a venlafaxine tablet using hydrogel technology was "impossible," and pursued that avenue no further.[21]

5. **Wyeth succeeded in developing extended-release venlafaxine using a preexisting process for making coated spheroids.**

Wyeth next decided to put venlafaxine in the dosage form it had successfully used with a different drug, also similar to venlafaxine, called REDACTED The REDACTED dosage form consisted of coated spheroids created by the process of "extrusion and spheronization."[23] This process creates spheroids having a core composed of a pharmaceutically active ingredient mixed with a matrix former/binder such as microcrystalline cellulose ("MCC").[24] First, the active ingredient is mixed with MCC and water to activate the binder and create an elastic mass that has a putty-like texture.[25] Second, this wet, putty-like mass is processed through an "extruder," a machine which presses the material through small holes in a metal plate, creating strands of

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[18] Ex. 10 REDACTED

[19] *Id.* at REDACTED

[20] Ex. 11 (U.S. Patent No. 6,274,171 B1 ("'171 Patent")) at 4:60-64.

[21] *Id.* at 10:53-55.

[22] REDACTED

REDACTED

[23]

[24] A matrix is a tightly-held, uniform mixture of material within which the drug is housed. Throughout this brief, the unwieldy term "microcrystalline cellulose" will be silently abbreviated "MCC."

[25] *See, e.g.*, Ex. 11 ('171 patent) at 1:37-58.

"extrudate" shaped like short pieces of spaghetti.[26] Third, the extrudate is placed in a "spheronizer," a machine consisting of a bowl with a grooved, rapidly rotating bottom.[27] In the spheronizer, frictional forces break the extrudate into uniform pieces and round them off into spheroids. A coating that slows the dissolution of the spheroids is then applied.[28]

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[26] *Id.*

[27] *Id.*

[28] *Id.*

REDACTED

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REDACTED

a. Wyeth used the same extension and spheronization technique it had used successfully

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35 REDACTED

36 REDACTED

37 REDACTED

38 REDACTED

39 REDACTED

40 REDACTED

41 REDACTE

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"HPMC.").

(Impax will refer to "hydroxypropylmethylcellulose" as

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Once the manufacture of spheroids moved out of the laboratory and onto larger-scale equipment, Wyeth learned that HPMC was not an essential ingredient: "Subsequent experiments carried out on Hutt and Nica extruders surprisingly demonstrated that acceptable, and even improved, spheroids could be made without the use of an hydroxypropylmethylcellulose."[45]

REDACTED

b. Wyeth based the coating on its propranolol product.

REDACTED Clark hit on the formula set forth in the patents: "from about 80% to about 90% by weight of film coating of ethyl cellulose, NF, and from about 10% to about 20% by weight of film coating of hydroxypropylmethylcellulose, USP."[48]

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[43] REDACTED

[44] REDACTED

[45] Ex. 11 ('171 Patent) at 6:6-11.

[46] REDACTED

[47] REDACTED

[48] Ex. 11 ('171 Patent) at 3:37-40: REDACTED This coating is very similar to that disclosed in the '475 patent for the extended release formulation of propranolol. Ex. 16 (U.S. Patent No. 4,138,475 ("'475 Patent")) at 1:58-63 ("The film coating may, for example, comprise 80 to 100% by weight of ethylcellulose and 20 to 0 % by weight of hydroxypropyl methylcellulose.").

[49] REDACTED

c.

REDACTED

B. The Alza extended-release venlafaxine formulation.

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Subsequently, on December 8, 1994, Alza published the details of Alza's extended-release venlafaxine formulation as an international patent application pursuant to the Patent

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Cooperation Treaty ("PCT"), No. WO94/27589.[56] The PCT application expressly disclosed an extended-release venlafaxine formulation that was "useful for antidepressant therapy" and "a method useful for antidepressant therapy by administering the controlled-release dosage form comprising the compound of the invention."[57] The PCT application further disclosed specific examples of formulations of the invention,

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Alza was ultimately granted United States Patent No. 6,440,457, covering its extended-release venlafaxine formulation. The sole claim recites:

> A method for administering a drug to the gastrointestinal tract of a human, wherein the method comprises: (a) admitting orally into the human a dosage form comprising [venlafaxine] which drug possess antidepressant therapy and the dosage form comprises a member selected from the group consisting of a sustained-release dosage form and a controlled-release dosage form; and, (b) administering the drug from the dosage form over an extended period of time in a therapeutically responsive dose to produce the antidepressant therapy.[61]

Alza asserted this patent against Wyeth, claiming that using Effexor XR infringes.[62] In response, on July 28, 2006, Wyeth requested that the PTO reexamine the '457 patent.[63] In its reexamination request, Wyeth argued that the '457 patent should never have issued, since it was anticipated by an earlier patent that disclosed an extended-release dosage form just like the one Alza used, except that it did not disclose the use of venlafaxine as the active pharmaceutical

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[56] Ex. 22 (Alza PCT Application).

[57] *Id.* at 1.

[58] *Id.* at 22-24 (Examples 1 and 2).

[59] – REDACTED

[60] *Id.* at 175:1-176:8.

[61] Ex. 24 (U.S. Patent No. 6,440,457) at 14:28-48.

[62] Ex. 25 (Complaint in *Alza v. Wyeth*, No. 9:06-cv-00156-RHC (E. D. Tex.)).

[63] Ex. 26 (7/28/06 Reexamination Request) at WYETH331-000015.

ingredient.[64] Alza had argued in the original examination proceeding that this earlier patent did not anticipate, since the "very high solubility" of venlafaxine rendered it unlike those drugs used with the dosage form in the past.[65] The examiner disagreed, holding that because the prior art dosage form could be used to deliver sodium nitrate, a drug with high solubility, "it will deliver venlafaxine." Despite this disagreement, the '457 patent ultimately issued after an appeal.[66]

In its reexamination request, Wyeth argues that the examiner's initial rejection—on the ground that an extended-release dosage form which can deliver one water soluble drug can be expected to deliver another—was the right result. While the reexamination is still ongoing, the PTO's initial office action ruled in favor of Wyeth, holding that a skilled artisan would be motivated to combine references to create an extended-release venlafaxine formulation for reasons well-known in the art:

> The artisan is motivated to provide sustained and controlled release dosage forms for any of the art recognized advantages that these formulations provide. In particular, Gupta teaches the advantages of reduced dosing frequency, better patient convenience and compliance, reduced GI side effects and other toxic effects, less fluctuating plasma drug levels, more uniform drug effect, and lesser total dose.[67]

Alza submitted a response to this Office Action on March 19, 2007, and awaits final action by the PTO.[68]

C. Wyeth's clinical trials confirmed the therapeutic effect of the extended release product.

Wyeth conducted clinical trials in order to gain FDA approval for Effexor XR. The three key studies are:

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[64] *Id.* at WYETH331-000022.

[65] *Id.* at WYETH331-000023.

[66] *Id.*

[67] Ex. 27 (February 16, 2007 Office Action in Reexamination Control No. 90/008,142) at 10.

[68] Ex. 28 (docket sheet in Reexamination Control No. 90/008,142).

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D. Wyeth's prosecution of the patents-in-suit.

Wyeth has asserted three patents in this case: U.S. Patent Nos. 6,274,171,[75] 6,403,120,[76] and 6,419,958.[77] The patents share a common specification and common inventors: each lists as its inventors Wyeth employees Deborah Sherman, John Clark, John Lamer, and Steven White.[78]

The patent begins by asserting that extended release formulations are conventionally

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[69] Ex. 29 (208 study) at WYETH004-013235.

[70] Ex. 30 (209 study) at WYETH004-014380.

[71] Ex. 31 (367 study) at WYETH004-015402.

[72] Ex. 32 (Deposition of Ronald Thisted) at 57:13-58:20.

[73] Ex. 43 (7/26/93 Derivan Memo.) at WYETH020-006616.

[74] Ex. 29 (208 study) at WYETH004-013318

[75] Ex. 11 ('171 Patent).

[76] Ex. 33 (U.S. Patent 6,403,120 ("'120 patent")).

[77] Ex. 34 (U.S. Patent 6,419.958 ("'958 Patent")).

[78] Ex. 11 ('171 Patent); Ex. 33 ('120 Patent); Ex. 34 ('958 Patent).

prepared using hydrogel tablet technology.[79] The patent recounts Sherman's "failed experiments" to make a hydrogel extended-release formulation,[80] and tells of Sherman's early failed attempts to make spheroids without using HPMC:

> Numerous spheroid formulations were prepared using different grades of microcrystalline cellulose and HPMC, different ratios of venlafaxine hydrochloride and filler, different binders such as PVP, methylcellulose, water, and polyethylene glycol of different molecular weight ranges in order to find a formulation which would provide a suitable granulation mix which could be extruded properly. In the extrusion process, heat buildup occurred which dried out the extrudate so much that it was difficult to convert the extruded cylinders into spheroids. Addition of HPMC 2208 to the venlafaxine hydrochloride-microcrystalline cellulose mix made production of spheroids practical.[81]

Wyeth contended in the specification that it was "completely unexpected" that an extended release formulation of venlafaxine could be made given the drug's high water-solubility.[82] The specification then explains how the inventors solved this purported problem: "[t]he formulations of this invention comprise an extended release formulation of venlafaxine hydrochloride comprising a therapeutically effective amount of venlafaxine hydrochloride in spheroids comprised of venlafaxine hydrochloride, MCC and, optionally, HPMC coated with a mixture of ethyl cellulose and HPMC."[83] The patent explains that other grades of MCC and HPMC maybe substituted "without changing the inventive concept."[84]

The specification asserts that administering the formulation of the invention offers patients two benefits. First, it asserts that "use of the one-a-day venlafaxine hydrochloride formulations of this invention reduces by adaptation, the level of nausea and incidence of emesis that attend the administration of multiple daily dosing."[85] Second, it contends that "[t]hrough administration of the venlafaxine formulation of this invention, there is provided . . . a method

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[79] Ex. 11 ('171 Patent) at 1:13-15. Citations to the common specification will be made to the '171 patent throughout.

[80] *Id.* at 6:6.

[81] *Id.* at 5:1-13.

[82] *Id.* at 4:57-60.

[83] *Id.* at 2:63-3:2.

[84] *Id.* at 4:44-48.

[85] *Id.* at 2:46-49.

for eliminating the sharp peaks and troughs (hills and valleys) in blood plasma drug levels induced by multiple daily dosing with conventional immediate release venlafaxine hydrochloride tablets."[86]

In the first (non-provisional) application in the chain that led to the issuance of the patents-in-suit, Wyeth initially proposed formulation claims that were explicitly limited to formulations of venlafaxine, MCC, and HPMC.[87] Wyeth also proposed method claims similar to those at issue here, which did not explicitly recite the ingredients of the formulation to be administered using the claimed method.[88]

The examiner found the method claims unpatentable over a prior art patent which explicitly disclosed administering venlafaxine in a "sustained oral administration form or time-release form, which may be used to spread the doseage [sic] over time, such as for once-a-day applications."[89] The examiner insisted that Wyeth make explicit that its method claims were limited to the formulations described in the specification.[90] Wyeth **agreed** that the method claims would be amended to make them depend from the narrow formulation claims.[91] The examiner made an amendment to the claims consistent with that agreement, and Wyeth had the opportunity to make a further amendment if it objected to the examiner's action. Wyeth acquiesced in the examiner's action, and the examiner then issued a Notice of Allowance.[92]

Instead of filing an amendment as the examiner had instructed, and without any

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[86] *Id.* at 2:23-28.

[87] Ex. 35 (excerpt from file history of U.S. Patent App. No. 08/821,137) at WYETH 002-000804-005. The optional nature of HPMC first appeared in U.S. Patent App. No. 08/964,328. Ex. 36 (excerpt from file history of U.S. Patent App. No. 08/964,328) at WYETH 002-000580-083.

[88] Ex. 35 (excerpt from file history of U.S. Patent App. No. 08/821,137) at WYETH 002-000804-005.

[89] *Id.* at WYETH002-000850 ("Agreed to amend claims 9 and 10 to depend from claim 1 to avoid rejection over Upton which discloses extended release venlafaxine at col 5, lines 25-27."); *see* Ex. 37 (U.S. Patent No. 5,506,270 ("'270 Patent")) at 5:25-27 (disclosing extended release venlafaxine, as cited by the examiner).

[90] Ex. 35 (excerpt from file history of U.S. Patent App. No. 08/821,137) at WYETH002-000850.

[91] *Id.*

[92] *Id.* at WYETH 002-000907.

explanation, Wyeth abandoned that application after the Notice of Allowance had issued and filed a new application which was assigned to a different examiner.[93] Wyeth then re-proposed method claims virtually identical to the original (unamended) claims from the earlier application.[94] Wyeth did not tell the new examiner about the prior application, nor that a different examiner had rejected virtually identical claims and that Wyeth had agreed to amend these claims in order to overcome the prior art. After another abandonment and re-filing, the new examiner allowed the method claims to issue.[95] Wyeth has never offered any explanation for this conduct.

E. Impax's ANDA

On December 15, 2005, Impax filed ANDA No. 78-057 with the FDA.

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F. The Prior Art

United States Patent No. 4,138,475 issued on February 6, 1979. It teaches an extended-release formulation of the drug propranolol. The formulation described in the '475 patent is the same as that described in the patents-in-suit, except for the substitution of a different active pharmaceutical ingredient: it is created by extrusion and spheronization,[98] uses MCC as a matrix,

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[93] *Id.* at WYETH 002-000911 (abandoning the '137 application, which was assigned to Examiner Hulina); Ex. 36 (excerpt from file history of U.S. Patent App. No. 08/964,328) at WYETH 002-000715-720 (indicating assignment of the '328 Application to Examiner Spear).

[94] Ex. 36 (excerpt from file history of U.S. Patent App. No. 08/964,328) at WYETH 002-000582.

[95] REDACTED

[96] Ex. 38 (excerpt from Impax ANDA listing ingredients in Impax's product) at IMPAX0003789-791.

[97] *Id.*

[98] Ex. 16 ('475 patent) at 2:10-16 ("For example, the spheroids may be manufactured on a

blended with the active pharmaceutical ingredient,[99] comprises spheroids coated with an extended-release mixture of ethylcellulose and HPMC,[100] and includes placing those spheroids in a capsule.[101]

United States Patent No. 4,535,186 was issued on August 13, 1985, and assigned to Wyeth. It teaches that venlafaxine is "useful in the treatment of depression, for which purpose they may be administered orally or parenterally in an amount sufficient to alleviate the symptoms of depression."[102] Venlafaxine may be "compounded into any of the usual oral dosage forms including tablets [and] capsules[.]"[103] The '186 patent is prior art under 35 U.S.C. § 102(a), since it describes an invention patented in the United States before the invention of the patents-in-suit.

Alza's international PCT application number WO 94/27589, filed on May 27, 1994, describes an extended-release formulation of venlafaxine. It is directed toward providing a "once-a-day controlled-release dosage form to deliver [venlafaxine] orally to a patient in need of therapy."[104] It teaches that one can "deliver the therapeutic drug in a therapeutically effective amount at a controlled rate over an extended period of time to the patient in need of said therapy."[105] The '589 application is prior art under at least 35 U.S.C. § 102(b), since the application was published on December 8, 1994, more than one year before the March 25, 1996

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conventional spheroniser in which a horizontal, rough-surfaced plate rotates inside a stationary vertical cylinder, and then film coated in conventional manner in a perforated coating drum, and finally the film coated spheroids filled into hard gelatine capsules using a conventional encapsulation machine.")

[99] *Id.* at 2:20-23 ("Propranolol hydrochloride (60kg.) and microcrystalline cellulose (Avicel-PH-101; 40kg.) were blended together in a 450 litre planetary mixer.")

[100] *Id.* at 1:33-36 ("the said spheroids having a film coat comprising ethylcellulose optionally together with hydroxypropyl methylcellulose").

[101] *Id.* at 2:15-16 ("finally the film coated spheroids filled into hard gelatine capsules using a conventional encapsulation machine.")

[102] Ex. 1 at 10:17-20.

[103] Ex. 1 at 10:34-35.

[104] Ex. 22 (Alza PCT Application) at 6:10-12.

[105] *Id.* at 27.

effective filing date of the patents-in-suit.[106]

United States Patent No. 5,506,270 was filed on January 30, 1995 and issued on April 9, 1996, and assigned to Wyeth. It describes a method of providing therapy by administering venlafaxine "in . . . sustained oral administration form or time-release form, which may be used to spread the dosage over time, such as for once-a-day applications."[107] The '270 patent is prior art under 35 U.S.C. § 102(e)(2), since it was filed on January 30, 1995, before the invention of the patents-in-suit, making it a "patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent."

G. The level of ordinary skill in the art.

There is no significant dispute about the level of ordinary skill in the art. According to Wyeth's expert, Dr. Sawchuk:

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III. STANDARD OF REVIEW[109]

Rule 56(c) of the Federal Rules of Civil Procedure provides that a party is entitled to summary judgment if a court determines from its examination of "the pleadings, depositions, answers to interrogatories, and admissions on file, together with the affidavits, if any," that there are no genuine issues of material fact and that the moving party is entitled to judgment as a matter of law. Fed. R. Civ. P. 56(c). In determining whether there is a triable dispute of material

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[106] *Id.* (cover page).

[107] Ex. 37 ('270 patent) at 5:25-27.

[108] Ex. 39 (excerpt from the expert report of Dr. Ronald Sawchuk) at 10-11.

[109] *Lacy v. Nat'l R.R. Passenger Corp.*, 507 F. Supp. 2d 438 (D. Del. 2007); *Harrison v. Christopher*, 489 F. Supp. 2d 375 (D. Del. 2007).

fact, a court must review all of the evidence and construe all inferences in the light most favorable to the non-moving party.[110]

To defeat a motion for summary judgment, the non-moving party must "do more than simply show that there is some metaphysical doubt as to the material facts . . . . In the language of the Rule, the non-moving party must come forward with specific facts showing that there is a genuine issue for trial."[111] But the mere existence of some evidence in support of the nonmovant will not be sufficient to support denial of summary judgment; there must be enough evidence to enable a jury to reasonably find for the nonmovant on that issue.[112] Thus, if the evidence is "merely colorable, or is not significantly probative," summary judgment is appropriate.[113]

IV. ARGUMENT

A. The preambles of the asserted claims do not limit claim scope.

The preamble of a patent claim consists of the words at the beginning of the claim that precede the transitional phrase (such as "comprising" or "which comprises").[114] "Preambles are used primarily to give the field within which the invention has utility."[115]

Here, each asserted method claim consists of (1) a preamble that describes the purpose of the alleged invention and (2) a claim body that sets forth the alleged invention itself. The preambles fall into two categories. First are preambles that describe the purpose of "providing a therapeutic blood plasma concentration of venlafaxine over a twenty four hour period with diminished incidence of nausea and emesis."[116] The second category of preambles describe the separate purpose of "eliminating the troughs and peaks of drug concentration attending the

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[110] *Valhal Corp. v. Sullivan Assocs., Inc.*, 44 F.3d 195, 200 (3d Cir. 1995).

[111] *Matsushita Elec. Indus. Co., Ltd. v. Zenith Radio Corp.*, 475 U.S. 574, 586-87 (1986) (internal quotations and citations omitted).

[112] *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 249 (1986).

[113] *Id.*

[114] *See generally, e.g., Allen Eng'g Corp. v. Bartell Indus., Inc.*, 299 F.3d 1336 (Fed. Cir. 2002).

[115] 1 DELLER, PATENT CLAIMS § 163 (2d ed. 1971).

[116] Ex. 11 ('171 Patent) Claims 20, 22, 23; Ex. 35 ('120 Patent) Claims 1, 2, 13, 14; Ex. 36 ('958 Patent) Claims 1, 3, 4.

therapeutic metabolism of plural daily doses of venlafaxine hydrochloride."[117]

The preambles should not be construed as limitations on the asserted claims. The Federal Circuit recognizes two circumstances in which preambles limit claim scope. Neither is present here. First, "a preamble limits the invention if it recites essential general structure or steps, or if it is 'necessary to give life, meaning, and vitality' to the claim."[118] For example, when the meaning of a term in the claim body depends on a phrase used in the preamble, the preamble may limit the claim scope "because it indicates a reliance on both the preamble and claim body to define the claimed invention."[119] "Likewise, when the preamble is essential to understand limitations of terms in the claim body, the preamble limits claim scope."[120] Second, where a patentee successfully distinguished over prior art by relying on the preamble, that "transforms the preamble into a claim limitation because such reliance indicates use of the preamble to define, in part, the claimed invention."[121] But "[w]ithout such reliance ... a preamble generally is not limiting when the claim body describes a structurally complete invention such that deletion of the preamble phrase does not affect the structure or steps of the claimed invention."[122] In other words, "preamble language merely extolling benefits or features of the claimed invention does not limit the claim scope without clear reliance on those benefits or features as patentably significant."[123]

The preambles to the asserted claims are not limiting under this test. First, nothing in the preambles recites an essential structure or step, or gives meaning to terms in the bodies of any of

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[117] Ex. 11 ('171 Patent) Claims 21, 24, 25; Ex. 36 ('958 Patent) Claims 2, 5, 6.

[118] *Catalina Mktg. Int'l, Inc. v. Coolsavings.com, Inc.*, 289 F.3d 801, 808 (Fed. Cir. 2002) (quoting *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1305 (Fed. Cir. 1999)).

[119] *Catalina*, 289 F.3d at 808.

[120] *Id.*

[121] *Id.*

[122] *Id.* at 809.

[123] *Id.; see also STX, LLC v. Brine, Inc.*, 211 F.3d 588, 591 (Fed. Cir. 2000) (preamble stating that invention provides "improved playing and handling characteristics" is not a limitation); *Bristol-Myers Squibb Co. v. Ben Venue Labs, Inc.*, 246 F.3d 1368, 1375 (Fed. Cir. 2001) (steps of claimed method performed in the same way regardless whether intended results described in preamble ultimately occur).

the asserted claims. Likewise, none of the terminology in the preambles is imported into, or is required to give meaning to the terms in the bodies of the claims, which simply disclose the administration of an encapsulated extended-release formulation of venlafaxine that provides peak blood-plasma levels within various specified time frames.

In *Bristol-Myers Squibb Co. v. Ben Venue Labs, Inc.*,[124] the Federal Circuit evaluated similar claims and concluded that the preambles of the relevant claims were not limiting. There, the claims were directed to a method for treating a cancer patient through a three-hour infusion of an anti-tumor medication, which method reduced blood toxicity compared to the previous twenty-four-hour infusion method. In other words, like the Wyeth patents, the Bristol-Myers patents claimed a method for administering a particular medical treatment with the intended benefit of reducing side effects associated with that treatment. Specifically, the claims at issue described a method "for reducing hematologic toxicity" and a method "for treating a cancer patient to effect regression of a taxol-sensitive tumor, said method being associated with reduced hematologic toxicity," which method comprised administering an anti-cancer medication in a particular way.[125] The court affirmed the trial court's ruling that the preambles "merely express[ed] a purpose of reducing hematologic toxicity relative to the toxicity experienced by a patient undergoing a twenty-four-hour infusion."[126] The court concluded the preambles were not limiting because "[t]he steps of the three-hour infusion method are performed in the same way regardless whether or not the patient experiences a reduction in hematologic toxicity."[127]

The same is true here. The preambles of the asserted claims merely express the purposes of reducing nausea and vomiting and eliminating troughs and peaks relative to the effects experienced by a patient taking immediate-release venlafaxine. Likewise, the steps of Wyeth's claimed method for administering venlafaxine to a patient in need thereof will be performed in

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[124] 246 F.3d 1368 (Fed. Cir. 2001).

[125] *Bristol-Myers*, 246 F.3d at 1371-72.

[126] *Id.* at 1375.

[127] *Id.*

the same way regardless whether or not nausea and vomiting is actually reduced, or troughs and peaks are actually eliminated, relative to immediate-release venlafaxine for any particular patient. (It would be odd indeed if infringement could only be determined on a case by case basis by monitoring whether a given patient actually experienced a reduction in nausea and emesis or by checking a given patient's blood levels to detect the elimination of multiple peaks and troughs.) *Bristol-Myers* controls this case and firmly establishes that the preambles do not limit the claim scope.

Second, at no point during the prosecution of the patents-in-suit did the PTO ever require Wyeth to add the preamble language to distinguish over prior art. Nor did Wyeth ever rely on the preamble language to distinguish over prior art. Even if Wyeth had added the preamble language as an argument for patentability, the Federal Circuit has made clear that "unsolicited assertions of patentability made during prosecution do not create a material claim limitation where we have determined that the language does not create one."[128] Here, as discussed above, the language of the preambles creates no limitation.

Wyeth undoubtedly will argue that the doctrine of claim differentiation requires the Court to read the preambles as limiting. But claim differentiation only creates a "presumption that each claim in a patent has a different scope."[129] The Federal Circuit confronted this precise issue in *Bristol-Myers* and "declin[ed] to blindly apply the doctrine in this case to supplant other canons of claim construction that compel[led]" the conclusion that the preambles were not limiting.[130]

Accordingly, because neither recognized basis for construing the preambles to limit claim scope is present here, this Court should rule that the preambles are not limiting.

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[128] *Bristol-Myers*, 246 F.3d at 1375.

[129] *Curtiss-Wright Flow Control Corp. v. Velan, Inc.*, 438 F.3d 1374, 1380 (Fed. Cir. 2006) (internal citations omitted).

[130] *Bristol-Myers*, 246 F.3d at 1376.

B. The Alza PCT application and the extended-release formulation disclosed therein are anticipatory prior art under Wyeth's construction of extended release formulation.

1. If the preambles are not limiting, the Alza art anticipates all the asserted claims.

As discussed above, Wyeth was not the first company to develop an extended-release formulation of venlafaxine.

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Then, on December 8, 1994, Alza disclosed its extended-release venlafaxine product in an international patent application published under the Patent Cooperation Treaty.[131] That PCT application anticipates all limitations of the asserted claims of the '958 Patent under 35 U.S.C. § 102(b), if the preambles of the asserted claims do not limit claim scope.

Section 102(b) provides that a patent is invalid if "the invention was . . . described in a printed publication in this or a foreign country, . . . more than one year prior to the date of the application for patent in this country . . . ."[132] The Alza PCT application was published on December 8, 1994, more than one year before the filing date of the patents in suit.

Asserted claims 1 through 6 of the '958 patent each contain four limitations: (1) the oral administration to a patient in need thereof; (2) of an extended release formulation; (3) that provides a peak blood-plasma level in from about 4 to about 8 hours, or from about 5 to about 8 hours, or in about 6 hours; and (4) contains venlafaxine hydrochloride as the active ingredient. The PCT application expressly discloses each of these limitations.

First, the PCT application discloses oral administration to a patient in need thereof. The application makes multiple references to the fact that the Alza formulation is intended to be administered orally.[133] Likewise, because "a patient in need thereof" is properly understood as a

[131] Ex. 22 (Alza PCT application).

[132] 35 U.S.C. § 102(b).

[133] Ex. 22 (Alza PCT application) at 16:20, 26:20, 33 (claim 6).

patient suffering from depression, the application expressly discloses that the Alza formulation is meant to be given to such patients. The application clearly states that the invention includes "a method useful for antidepressant therapy by administering the controlled-release dosage form comprising the compound of the formula."[134] Further, the application states that the goal of the Alza invention is "to provide a therapeutic dose of [venlafaxine] in the body."[135] There can be no dispute that the application expressly and publicly disclosed that the Alza formulation was to be given orally to patients in need of an antidepressant.

Second, under Wyeth's proposed claim construction, the Alza formulation described in the PCT application expressly qualifies as an "extended release formulation"—"a formulation, other than a hydrogel tablet, which releases the active ingredient at a slower rate than the immediate release formulation of the active ingredient such that the dosing frequency is once-a-day rather than the plural daily dosing for the immediate release formulation." The Alza formulation as described in the PCT application is not a hydrogel tablet; it releases venlafaxine more slowly than the immediate-release Wyeth product; and it is intended to be given to patients once a day.[136]

Third, the PCT application discloses two examples

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[134] *Id.* at 1.

[135] *Id.*

[136] *Id.* at 3-4 (Alza drug designed to "eliminate the need for multiple dosing").

[137] Ex. 23 (Edgren Depo.) at 174:9-24.

[138] *Id.* at 175:1-176:8.

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Fourth, there is no dispute that the Alza invention disclosed in the PCT application used venlafaxine hydrochloride as its active ingredient.

Because each of the limitations of the asserted claims (exclusive of their preambles) is present in the Alza formulation described in the PCT application, the PCT application anticipates the asserted claims of the '958 patent, rendering them invalid under 35 U.S.C. § 102(b).

2. If the preambles are limiting, but the Court adopts Impax's construction of "eliminating the troughs and peaks of drug concentration in a patient's blood plasma," then the Alza art anticipates those claims as well.

Even if the preambles do limit claim scope, the Alza art would anticipate claims 2, 5, and 6 of the '958 patent under Impax's claim construction of "eliminating the troughs and peaks of drug concentration in a patient's blood plasma." Under Impax's construction, this phrase simply means the elimination of "the peak(s) and trough(s) due to the 'therapeutic metabolism' of any second or third dose given in a single day is eliminated by dosing only once every 24 hours"—in other words, moving from the multiple troughs and multiple peaks of blood-plasma concentration associated with multiple daily doses to a single trough and single peak associated with a single dose. Any single daily-dose extended-release formulation inherently would result in only one trough and one peak and thus "eliminate troughs and peaks." The PCT application expressly discloses the invention's method for achieving this result: maintaining a consistent blood-plasma level, as opposed to the variable blood-plasma level resulting from multiple daily

[139] Ex. 21 (134 Study) at WYETH022-001736

[140] *Id.* at WYETH022-001763.

dosing.[141]

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C. The patents-in-suit are invalid for obviousness.

A patent is invalid for obviousness where "the differences between the subject matter" claimed in the patent "and the prior art are such that the subject matter as a whole would have been obvious to a person having ordinary skill in the art."[143] Obviousness is a question of law.[144] That conclusion turns on the factors set out in *Graham v. John Deere Co.*[145]: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed subject matter and the prior art; and (4) secondary considerations of non-obviousness, such as commercial success or unexpected results.[146]

Earlier this year, in *KSR International Co. v. Teleflex Inc.*,[147] the Supreme Court affirmed a district court's grant of summary judgment of obviousness, reaffirming that obviousness is a question of law. In doing so, the Court emphasized that the obviousness inquiry is pragmatic and flexible: "The obviousness analysis cannot be confined by a formalistic conception of the words teaching, suggestion, and motivation, or by overemphasis on the importance of published articles and the explicit content of issued patents."[148] Instead, the Supreme Court urged a "common sense" approach to the use of customary knowledge in the obviousness equation: "A person of ordinary skill is also a person of ordinary creativity, not an automaton."[149] In this vein, the

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[141] Ex. 22 (Alza PCT application) at 3 (disclosing an improvement over "conventional dosage forms" which "produce [a] peaks and valleys drug pattern"); *see also generally id.* at 2-5.

[142] Ex. 23 (Edgren Depo.) at 138:16-139:5.

[143] 35 U.S.C. § 103; *Forest Labs., Inc. v. Ivax Pharms., Inc.*, 438 F. Supp. 2d 479, 496 (D. Del. 2006), *aff'd*, 501 F.3d 1263 (Fed. Cir. Sept. 5, 2007).

[144] *Phillips v. AWH Corp.*, 415 F.3d 1303, 1333 (Fed. Cir. 2005).

[145] 383 U.S. 1 (1966)

[146] *Id.* at 17-18.

[147] 127 S.Ct. 1727 (2007).

[148] *KSR*, 127 S. Ct. at 1741.

[149] *Id.* at 1742.

Supreme Court recognized that an "invention" is obvious where it consists of a combination of prior art that would have been obvious to try to a person of ordinary skill in the art:

> Where there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103.[150]

Since *KSR*, subsequent Federal Circuit cases have employed this common sense approach to determining obviousness. For instance, in *Aventis Pharma Deutschland GmbH v. Lupin, Ltd.*,[151] the concentration and purification of a known mixture using a known technique was found obvious.[152] Other post-*KSR* decisions have adopted the same analysis and reached similar results.[153]

On October 10, 2007, the PTO issued Guidelines "to assist Office personnel to make a proper determination of obviousness under 35 U.S.C. 103, and to provide a supporting rationale in view of" *KSR*.[154] In the Guidelines, the PTO articulates seven separate bases for a finding of obviousness. One of those bases is based directly on the language from *KSR* quoted above: "'Obvious To Try'—Choosing From a Finite Number of Identified, Predictable Solutions, With a Reasonable Expectation of Success."[155] To reject a claim as "obvious to try," the PTO Guidelines tell examiners to articulate: "(1) a finding that at the time of the invention, there had been a recognized problem or need in the art, which may include a design need or market

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[150] *Id.*

[151] 499 F.3d 1293 (Fed. Cir. 2007).

[152] *Aventis*, 499 F.3d at 1301.

[153] *See Leapfrog Enters., Inc. v. Fisher-Price, Inc.*, 485 F.3d 1157 (Fed. Cir. 2007); *Takeda Chemical Indus. Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350 (Fed. Cir. 2007); *PharmaStem Therapeutics, Inc. v. ViaCell, Inc.*, 491 F.3d 1342 (Fed. Cir. 2007); *In re Icon Health & Fitness, Inc.*, 2007 WL 2189161 (Fed. Cir. Aug. 1, 2007).

[154] Ex. 41 (United States Patent and Trademark Office, *Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 in View of the Supreme Court Decision in* KSR International Co. v. Teleflex Inc., 72 Fed. Reg. 57526 (Oct. 10, 2007)).

[155] *Id.* at 57532.

pressure to solve a problem; (2) a finding that there had been a finite number of identified, predictable potential solutions to the recognized need or problem; (3) a finding that one of ordinary skill in the art could have pursued the known potential solutions with a reasonable expectation of success; and (4) whatever additional findings based on the Graham factual inquiries may be necessary, in view of the facts of the case under consideration, to explain a conclusion of obviousness."[156] In setting forth these Guidelines, the PTO relies on the "obvious to try" analysis in two drug cases analyzed in detail below, *Alza Corporation v. Mylan Laboratories, Inc.* and *Pfizer, Inc. v. Apotex, Inc.*[157]

If the Court adopts Impax's construction of "extended release formulation," Impax must show only that Wyeth's particular formulation, which meets all of the asserted claims, was obvious. If the Court adopts Wyeth's construction of "extended release formulation," Impax must show even less: that some extended release formulation of venlafaxine meeting the asserted claims, other than a hydrogel tablet, would have been obvious.

1. All of the elements of the invention were known in the prior art.

Graham requires that the court consider similarities or differences "between the claimed subject matter and the prior art."[158] Here, all of the elements of the invention were known in the prior art, and all that remained was for a skilled artisan to combine them to make the claimed invention.

a. The elements of Wyeth's particular formulation were well known in the art.

As described above in Part II.D, Wyeth's "invention" consists of a specific formulation: venlafaxine hydrochloride in encapsulated, coated spheroids containing MCC with optional HPMC. Both the active pharmaceutical ingredient, venlafaxine, and the dosage form in which the venlafaxine was placed were well known in the prior art long before the application date.

First, at the time of the alleged invention, it is undisputed that venlafaxine was known in

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[156] *Id.*

[157] *Id.* (citing *Alza*, 464 F.3d 1286 (Fed. Cir. 2006) and *Pfizer*, 480 F.3d 1348 (Fed. Cir. 2007)).

[158] 383 U.S. at 17-18.

the art: Wyeth had patented it in 1983, by U.S. Patent No. 4,535,186. Second, the particular extended-release technique eventually used to create Effexor XR was also well-known. U.S. Patent No. 4,138,475 (issued Feb. 6, 1979) describes an extended-release formulation technique of placing an active pharmaceutical ingredient—in that case, propranolol hydrochloride—in encapsulated, coated spheroids containing MCC.[159]

The formulation described in the patents-in-suit is the same as that described in the '475 patent, with one exception: the substitution of the active ingredient venlafaxine hydrochloride for propranolol hydrochloride. Both the '475 patents and the patents-in-suit disclose extrusion and spheronization.[160] They both use MCC as a matrix blended with the active pharmaceutical ingredient.[161] They both produce spheroids coated with an extended-release mixture of ethylcellulose and HPMC,[162] and they both place those spheroids in a capsule.[163]

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[159] *See* Ex. 16 ('475 patent) at 1:26-36 (teaching a "sustained release pharmaceutical composition consisting of a **hard gelatine capsule containing film coated spheroids**, the said spheroids comprising, prior to coating, 40 to 65% by weight of propranolol or a pharmaceutically-acceptable acid-addition salt thereof in admixture with non-water-swellable **microcrystalline cellulose**, and the said spheroids having a film coat comprising ethylcellulose optionally together with hydroxypropyl methylcellulose.")

[160] *Id.* at 2:10-16.

[161] *Id.* at 2:20-23 ("Propranolol hydrochloride (60kg.) and microcrystalline cellulose (Avicel-PH-101; 40kg.) were blended together in a 450 litre planetary mixer.")

[162] *Id.* at 1:33-36 ("the said spheroids having a film coat comprising ethylcellulose optionally together with hydroxypropyl methylcellulose").

[163] *Id.* at 2:15-16 ("finally the film coated spheroids filled into hard gelatine capsules using a conventional encapsulation machine.")

[164]

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Because the formulation described in the patents-in-suit is nothing more than the combination of the active ingredient disclosed in the '186 patent with the formulation disclosed in the '475 patent, the prior art renders obvious the particular formulation described in the patents-in-suit.

b. The known benefits of once-daily dosing provide the necessary "design need or market pressure."

Under *KSR Intern. Co. v. Teleflex, Inc.*, "any need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed."[167] Here, there is no dispute that a person of ordinary skill in the art would have known of the problem that multiple daily dosing is inconvenient for patients.[168]

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A person of skill in the art would have been motivated to combine prior art references to create a once-daily venlafaxine formulation because of the known desire to increase patient convenience.

c. The handful of well-known extended-release formulation techniques provided "a finite number of identified, predictable solutions."

Under *KSR*, subject matter is obvious when it results from the successful pursuit of "a finite number of identified, predictable solutions."[170] There were a "finite number" of solutions to Wyeth's problem.

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there are just a handful of well-known formulation techniques, among them hydrogel tablets and encapsulated spheroids created through extrusion and

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[165] *See* Part II.A.5.a, *supra.*

[166] Ex. 9 (Sherman Depo.) at 48:20-49:9.

[167] 127 S.Ct. at 1742.

[168] Ex. 4 (Salinas Depo.) at 85:24-86:4.

[169] Ex. 5 (Enever Depo.) at 89:8-19.

[170] *KSR*, 127 S.Ct. at 1742.

spheronization.[171] Wyeth pursued each of this handful of well-known approaches in turn; when its first approach did not succeed, it turned to a second approach, which did. Indeed, as the patents recite, "Where the production of tablets is not feasible, it is conventional in the drug industry to prepare encapsulated drug formulations which provide extended or sustained release properties."[172]

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These solutions were, in *KSR*'s terms, "identified;"

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Thus, the prior art provided Wyeth with a finite number of identified solutions to the problem of formulating extended-release venlafaxine.

2. There was a reasonable expectation of success.

In order for a patent to be obvious, a person of ordinary skill must be shown to have been able to undertake the project of combining the prior art references with a "reasonable expectation of success."[174] The requisite "reasonable expectation of success" does not require a guarantee or absolute certainty, and some degree of unpredictability in the art does not avoid an obviousness determination.[175] A patentee's statements that a particular approach was expected to work are highly probative of a reasonable expectation of success.[176]

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[171] *Supra* section II.A.4-5.

[172] Ex. 11 ('171 patent) at 1:35-38.

[173] REDACTED

[174] *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1361 (Fed. Cir. 2007).

[175] *Pfizer*, 480 F.3d at 1364; *PharmaStem Therapeutics, Inc. v. Viacell, Inc.*, 491 F.3d 1342, 1363-64 (Fed. Cir. 2007) ("[T]he inventors merely used routine research methods to prove what was already believed to be the case. Scientific confirmation of what was already believed to be true may be a valuable contribution, but it does not give rise to a patentable invention.").

[176] *Pfizer*, 480 F.3d at 1365.

In *Alza Corp. v. Mylan Labs., Inc.*,[177] the Federal Circuit evaluated a patent strikingly similar to the one here, and held it obvious over three prior art patents. There, the first of the prior art patents claimed a "sustained-release pharmaceutical composition including an active ingredient of high solubility in water" where the drug's dissolution rate could be modified at will.[178] The second prior art patent claimed a 24-hour oxybutynin formulation using a coating similar to the accused product, and taught methods of modifying the dosage forms to slow release rates. A third prior art patent taught a particular sustained release system to deliver any drug over a 24 hour period, including categories of drugs of which oxybutynin was a member. The Federal Circuit held that the patent in suit was invalid as obvious, over the plaintiff's argument that there would have been no reasonable expectation of success. The court held that where a prior art patent taught "ways of achieving slow rates of release," combining those formulation methods with a known pharmaceutical ingredient could be pursued with a reasonable expectation of success, particularly where there was suggestion in the prior art that previous attempts to achieve a slow release of the same drug had been successful.[179]

Likewise, here, the undisputed facts show that Wyeth had a reasonable expectation of success.

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Because a person of ordinary skill in the art would have been motivated to combine the

[177] 464 F.3d 1286, 1292 (Fed. Cir. 2006).

[178] *Id.* at 1292.

[179] *Id* at 1293.

[180] REDACTED

[181] REDACTED

'186 and '475 references with a reasonable expectation of success, Wyeth's particular extended-release venlafaxine formulation was obvious.

Wyeth maintains that because the action of any drug formulation in humans cannot be predicted with absolute certainty until that drug formulation is tested in humans, the inventors of the patents-in-suit could not have had a reasonable expectation of success.[182] This argument fails under the Federal Circuit's obviousness jurisprudence, as illustrated by *Pfizer Inc. v. Apotex, Inc.*[183]

In *Pfizer*, the patent in suit claimed the besylate salt of a drug called amlodipine, which could be used to treat hypertension, ischemia, and angina.[184] Pfizer contended that the selection of the besylate salt (as opposed to other salts, such as the hydrochloride) was non-obvious, because "choosing an appropriate salt is a difficult task since each salt imparts unique properties to the parent compound."[185] Those properties, Pfizer argued, could not be determined beforehand; each particular salt had to be manufactured and tested.[186] Thus, Pfizer argued, "the skilled artisan would have had no expectation of success in making a besylate salt of amlodipine because there was no reliable way to predict the influence of a particular salt species on the active part of the compound."[187]

The Federal Circuit disagreed, holding Pfizer's patent invalid for obviousness. The "case law is clear," the court held, "that obviousness cannot be avoided simply by a showing of some degree of unpredictability in the art so long as there was a reasonable probability of success."[188] Knowledge in the prior art had allowed Pfizer to narrow the range of likely candidates to just nine salts for testing—the maleate, acetate, succinate, besylate, mesylate, tosylate, salicylate, and

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[183] 480 F.3d 1348 (Fed. Cir. 2007).

[184] *Pfizer*, 480 F.3d at 1356.

[185] *Id.* at 1355 (internal quotation omitted).

[186] *Id.*

[187] *Id.* at 1364.

[188] *Id.*

hydrochloride.[189] Merely testing each in turn "by routine procedures to verify its expected properties," the court held, was obvious, even though the results of any particular test could not be predicted ahead of time.[190] "Indeed, a rule of law equating unpredictability to patentability, applied in this case, would mean that any new salt—including those specifically listed in the [prior art]—would be separately patentable, simply because the formation and properties of each salt must be verified through testing. This cannot be the proper standard since the expectation of success need only be reasonable, not absolute."[191]

Here, as in *Pfizer*, the court faces a claim of patent rights over an "invention" that was obvious from the prior art but whose utility was not certain until it was tested. Until it was given to a human, Wyeth contends, the inventors of the patents in suit could not have known that their formulation would be therapeutically effective.[192] But here, as in *Pfizer*, there were a small number of approaches for Wyeth to pursue. Instead of manufacturing and testing nine salts of amlodipine, Wyeth had to manufacture and test a handful of extended-release formulations of venlafaxine. Just as Pfizer quickly hit upon an amlodipine salt that "would work for its intended purpose,"[193] Wyeth quickly hit upon an extended-release formulation of venlafaxine that was therapeutically effective. As the court in Pfizer held, merely *verifying* that something has the desired properties is "not equivalent to the trial and error procedures often employed to *discover* a new compound where the prior art gave no motivation or suggestion to make the new compound nor a reasonable expectation of success."[194]

The undisputed evidence shows that a person of ordinary skill in the art would have expected that at least one of the handful of known approaches to making extended-release formulations would work to create an extended-release venlafaxine formulation. The prior art

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[189] *Id.* at 1354.

[190] *Id.* at 1365.

[191] *Id.* at 1364.

[192] Ex. 45 (Wyeth response to Impax Interrogatory No. 28) at 25.

[193] *Pfizer*, 480 F.3d at 1365

[194] *Id.* at 1367 (emphasis in original).

'270 patent taught that venlafaxine could provide therapy when "provided in . . . sustained oral administration form or time-release form, which may be used to spread the doseage over time, such as for once-a-day applications."[195] To be sure, the effectiveness of such formulations would still need to be "verified through testing,"[196] but the prior art clearly teaches that *one* of the usual approaches to making an extended-release formulation would work.

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(i) Therapeutic effectiveness.

The prior art taught that an extended-release venlafaxine formulation could be reasonably expected to be therapeutically effective, and Wyeth's own documents show that the inventors in fact possessed such a reasonable expectation. Accordingly, because the prior art taught the therapeutic qualities of venlafaxine and taught that drugs such as venlafaxine would remain therapeutic when integrated into an extended-release formulation with a reasonable expectation of success, the patents-in-suit are invalid as obvious.

It is undisputed that the therapeutic effect of an extended-release venlafaxine formulation was taught by the prior art. First, the PCT application alone explicitly teaches that one can "deliver [venlafaxine] in a therapeutically effective amount at a controlled rate over an extended period of time to the patient in need of said therapy."[200] The very first page of the PCT

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[195] Ex. 37 ('270 patent) at 5:25-27.

[196] *Pfizer*, 480 F.3d at 1364.

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[198] REDACTED

[199] *Pfizer* at 1354.

[200] Ex. 22 (Alza PCT Application) at 27.

application states that "[t]he primary goal of drug administration is to provide a therapeutic dose of drug in the body to achieve a desired blood concentration, and then maintain the desired drug blood concentration."[201] Similarly, the application makes clear the invention is designed to maintain that blood concentration over a full day, in order to prevent "dos[ing] twice or thrice a day" and "eliminate the need for multiple dosing."[202]

Second, one of Wyeth's own prior art venlafaxine patents discloses the therapeutic efficacy of extended-release venlafaxine. The '270 patent discloses a method of providing therapy for hypothalamic amenhorrhea using extended-release venlafaxine. That patent explicitly discloses that therapy can be achieved by administering venlafaxine "in . . . sustained oral administration form or time-release form, which may be used to spread the dosage over time, such as for once-a-day applications."[203] Far from being inventive, the therapeutic efficacy of once-a-day venlafaxine is explicitly recited in the prior art.

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(ii) Blood plasma levels, including elimination of peaks and troughs.

Some of the asserted claims recite specific times to peak blood plasma levels, specific blood plasma levels, or (if the preambles are limiting) the fact that the blood plasma curves for extended-release venlafaxine contain fewer "peaks and troughs" than the blood plasma curves for immediate-release venlafaxine. Each of these relates to the shape of the graph of blood plasma level of venlafaxine over time, and each is present in the prior art. The target dissolution profiles were not inventive, and Wyeth had a reasonable expectation of success in achieving

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[201] *Id.* at 1.

[202] *Id.* at 3-4.

[203] Ex. 37 ('270 patent) at 5:25-27.

[204] Ex. 9 (Sherman Depo.) at 58:12-22.

[205] Ex. 5 (Enever Depo.) at 312:7-15.

them.

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(iii) Reduction in incidence of nausea and emesis.

If the preambles of the claims are limiting, then some of the asserted claims require a reduction in incidence of nausea and emesis. Here, too, Wyeth reasonably expected to achieve this result.

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3. Because the asserted claims are invalid for obviousness under Impax's claim construction, they are necessarily invalid for obviousness under Wyeth's broad claim construction.

Because the prior art taught how to make Wyeth's particular encapsulated extended-

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release formulation, the inquiry under Wyeth's proposed claim construction is even more straightforward, because all that must be shown is that it was obvious for Wyeth to make any extended release formulation. Indeed, Wyeth's request for reexamination of the Alza patent makes exactly this point. The reexamination request asserts that the claim in Alza's '457 patent is invalid because it is indistinguishable from the combination of two rejected Alza divisional applications of the '457: (1) the '292 application, which recites a dosage form for delivery of venlafaxine, and (2) the '370 application, which recites a "controlled-release dosage form" (claim 9) and a "sustained-release dosage form" (claim 15) of venlafaxine.[216] In other words, Wyeth has taken the position that the combination of venlafaxine—a known antidepressant—with extended-release technology—a known dosage delivery form—is obvious and unpatentable.[217] That same logic applies equally to Wyeth's patents, and invalidates them for obviousness.

4. Because Wyeth held the patent on the venlafaxine molecule, no other company could develop an extended-release venlafaxine product, and thus the secondary considerations of non-obviousness are of little weight.

Wyeth holds a patent on the venlafaxine molecule itself. That patent is still in effect today. Without a license from Wyeth, no company can market any product containing venlafaxine, extended-release or otherwise. Wyeth's Effexor XR product has brought it substantial revenue, and in other cases that commercial success might bolster Wyeth's claims of nonobviousness. But because Wyeth had the exclusive right to market venlafaxine products, the fact that no other company brought an extended-release venlafaxine product to market sooner, or that there may have been a need in the market for such a product, says nothing about the nonobviousness of the asserted claims.

Courts sometimes consider commercial success and other "secondary considerations of non-obviousness" in determining whether a patent is invalid as obvious.[218] "Commercial success

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[216] Ex. 26 (July 28, 2007 Reexamination Request) at WYETH331-000035.

[217] *Id.*

[218] *See, e.g., Graham v. John Deere Co*, 383 U.S. 1, 17-18.

is relevant because the law presumes an idea would successfully have been brought to market sooner, in response to market forces, had the idea been obvious to persons skilled in the art."[219] This "chain of inferences," leads from the commercial success of the patented product to the inference that "attempts [by other would-be innovators] have been made and have failed."[220]

For example, in *Merck*, the plaintiff owned two patents. The first, the '077 patent, claimed a method of treating osteoporosis "which consists of administering to a patient in need thereof an effective amount of" a drug marketed under the name Fosamax.[221] The second, the '329 patent, claimed a method of treating osteoporosis "comprising orally administering about 70 mg of [Fosamax] . . . having a dosing interval of once-weekly."[222]

Teva, a maker of generic drugs, filed an ANDA seeking to make a generic version of Fosamax. Merck asserted only the '329 patent against Teva: because it was filed later, the '329 patent would expire much later than the '077 patent, and would thus keep Teva out of the market longer.[223] Teva asserted that the '329 patent was invalid for obviousness, based on two articles published after the '077 was issued but before the invention date of the '329 suggesting that lessening dosing frequency might ameliorate some of the side effects of the formulation described in the '077 patent.[224]

In attempting to rebut Teva's obviousness argument, Merck pointed to the commercial success of its once-a-week formulation.[225] But the Federal Circuit found that although "Merck's once-weekly dosing of Fosamax was commercially successful, in this context that fact has minimal probative value on the issue of obviousness."[226] Because the '077 patent prevented any

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[219] *Merck & Co., Inc. v. Teva Pharms. USA, Inc.*, 395 F.3d 1364, 1376 (Fed. Cir. 2005).
[220] *Id.* at 1376-77 (internal quotation omitted).
[221] *Id.* at 1377.
[222] *Id.* at 1366.
[223] *Id.* at 1367.
[224] *Id.* at 1375-76.
[225] *Id.* at 1376.
[226] *Id.*

competitor from marketing any formulation of Fosamax—daily, weekly, or otherwise—the court held that the link between commercial success and nonobviousness "has no force in this case."[227] Where "others were legally barred from commercially testing" the idea, "that chain of inferences" leading from commercial success to the failures of others to nonobviousness "fails."[228] Even if there was money to be made, and all of the technical problems could be solved by a person of ordinary skill in the art, no third party could enter the market and make that money. When "market entry by others was precluded," the Federal Circuit held, the "inference of non-obviousness" from "evidence of commercial success, is weak."[229]

Here, as in *Merck*, the plaintiff owns a soon-to-expire patent on a drug substance—the '186 patent—and much younger patents on a commercially successful method of administering an extended-release formulation of that drug substance—the patents in suit. The '186 patent prevented anyone from making an extended-release venlafaxine formulation without Wyeth's permission. Thus, the fact that no company other than Wyeth developed a commercially successful extended-release venlafaxine formulation is not attributable to the non-obviousness of the patents-in-suit, but instead to the fact that others were legally barred from doing so. Accordingly, secondary considerations such as the commercial success Effexor XR has enjoyed, or the need for an extended release formulation of venlafaxine, cannot furnish proof of nonobviousness.

V. CONCLUSION

For all the foregoing reasons, the Court should rule that Wyeth's patents are invalid, and grant summary judgment in favor of Impax.

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[227] *Id.*

[228] *Id.* at 1376-77.

[229] *Id.*

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